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Full Length Article

Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy

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ABSTRACT

Background: Few data are available on the rate and characteristics of thromboembolic complications in hospitalized patients with COVID-19.

Methods: We studied consecutive symptomatic patients with laboratory-proven COVID-19 admitted to a university hospital in Milan, Italy (13.02.2020–10.04.2020). The primary outcome was any thromboembolic complication, including venous thromboembolism (VTE), ischemic stroke, and acute coronary syndrome (ACS)/myocardial infarction (MI). Secondary outcome was overt disseminated intravascular coagulation (DIC).

Results: We included 388 patients (median age 66 years, 68% men, 16% requiring intensive care [ICU]). Thromboprophylaxis was used in 100% of ICU patients and 75% of those on the general ward. Thromboembolic events occurred in 28 (7.7% of closed cases; 95%CI 5.4%–11.0%), corresponding to a cumulative rate of 21% (27.6% ICU, 6.6% general ward). Half of the thromboembolic events were diagnosed within 24 h of hospital admission. Forty-four patients underwent VTE imaging tests and VTE was confirmed in 16 (36%). Computed tomography pulmonary angiography (CTPA) was performed in 30 patients, corresponding to 7.7% of total, and pulmonary embolism was confirmed in 10 (33% of CTPA). The rate of ischemic stroke and ACS/MI was 2.5% and 1.1%, respectively. Overt DIC was present in 8 (2.2%) patients.

Conclusions: The high number of arterial and, in particular, venous thromboembolic events diagnosed within 24 h of admission and the high rate of positive VTE imaging tests among the few COVID-19 patients tested suggest that there is an urgent need to improve specific VTE diagnostic strategies and investigate the efficacy and safety of thromboprophylaxis in ambulatory COVID-19 patients.

1. Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) causing coronavirus disease 2019 (COVID-19) has led to an unprecedented global health crisis. To date, > 185,000 COVID-19-related deaths have been confirmed. Case fatality rate has been estimated to be as high as 15% in some countries [1].

Clinical manifestations are absent or mild in a substantial proportion of subjects who test positive for SARS-CoV2. Bilateral pneumonia is the main finding in hospitalized patients and at least 5% initially present in serious condition, requiring advanced medical support or intensive care [1,2]. Bilateral pneumonia, systemic inflammation, endothelial dysfunction, coagulation activation, acute respiratory distress syndrome, and multiorgan failure have been described as key features of severe COVID-19 [3–8]. Signs of myocardial injury are present in at least one quarter of severe cases [2,9].

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It has been postulated that the high mortality observed among COVID-19 patients may be partly due to unrecognized pulmonary embolism (PE) and pulmonary *in situ* thrombosis. Estimates of the risk of arterial and, in particular, venous thromboembolic complications are still preliminary and depend on local diagnostic and pharmacological preventive strategies [10,11].

Better understanding of COVID-19-related thromboembolic risk will help to optimize diagnostic strategies and guide the design and conduction of randomized controlled trials on VTE prevention. In this study, we described the rate and characteristics of venous and arterial thromboembolic complications in consecutive patients who have been admitted to a large academic hospital in Milan, Italy, since the beginning of the outbreak.

2. Methods

2.1. Setting and study population

In this retrospective cohort study, we included data from consecutive adult symptomatic patients with laboratory-proven COVID-19 who have been admitted to a large university hospital (Humanitas Clinical and Research Hospital, Rozzano, Milan, Lombardy, Italy) since February 2020. The study was approved by the institutional ethical committee and patients gave standard written consent to the use of their data.

2.2. Objectives

We aimed to describe the rate of venous and arterial thromboembolic complications in hospitalized patients with COVID-19.

2.3. Data collection

Electronic medical records served as source data for the collection of demographics, clinical, laboratory, treatment, and outcome data, which were extracted in an anonymized form by two physicians. Potential disagreements concerning the interpretation of the findings was done in collaboration with a third physician.

2.4. Outcomes

The primary outcome was a composite of venous and arterial thromboembolic events, encompassing VTE and other cardiovascular events. VTE included pulmonary embolism (PE) and deep vein thrombosis (DVT) diagnosed by accepted imaging tests. During the period considered for the present analysis, no VTE screening strategy among COVID-19 patients was in place at the study site: VTE imaging tests were performed in subjects with signs or symptoms of DVT or with an unexplained clinical worsening of the respiratory function, primarily assessed using the PaO_2/FIO_2 ratio, or a rapid increase of D-dimer levels. Two-point compression ultrasonography (CUS) was used on the intensive care unit (ICU); whole-leg ultrasound was performed in symptomatic patients on the general ward. Cardiovascular events included acute coronary syndrome/myocardial infarction and ischemic stroke, as reported by the treating physicians in the medical charts.

Secondary outcome was overt disseminated intravascular coagulation (DIC). We reviewed the electronic medical charts and patients´ laboratory findings (platelet count, D-dimer, prothrombin time, fibrinogen level) of all COVID-19 patients to retrospectively calculate the International Society on Thrombosis and Haemostasis (ISTH) score for overt DIC, which was considered present if the score was 5 or greater [12].

2.5. Statistical methods

We described the characteristics of our study population using counts and percentages for categorical variables. We used appropriate measures of central tendency and dispersion to describe continuous variables. The rate of events was accompanied by 95% confidence interval (95%CI) and calculated for closed cases, defined as patients discharged, or dead, or (for analysis on thromboembolic complications) diagnosed with a thromboembolic event. Cumulative rates were calculated for the whole study population, including patients still hospitalized. A univariate logistic regression was performed to ascertain the effects of age on the likelihood that patients died during hospitalization: the probability of death across age was depicted visually. Missing values have been reported for each variable, if any. JASP v.0.11.1 and SPSS v. 25.0 served for data analysis.

3. Results

We extracted data from 388 consecutive patients with laboratory-proven COVID-19 admitted between 13.02.2020 and 10.04.2020. The median age was 66 (Q1-Q3 55–85) years and 264 (68%) were men. A total of 375 (97%) patients were tested for SARS-CoV2 before or on the day of initial hospital admission. Eight (2.1%) patients were tested during the first week of hospitalization and six (1.5%) between week 2–4 of hospitalization. Patients admitted to hospital during the very first days of the outbreak belonged to the latter group.

A total of 61 (16%) patients required intensive care; the remaining 327 patients were admitted to general wards. Of 61 patients who required intensive care, 30 (49%) were initially admitted to a general ward for a median of 4 (Q1-Q3 3–6) days; the median length of stay in the ICU was 12 (Q1-Q3 8–15) days. Table 1 summarizes the baseline characteristics of the study population, including the overall duration of hospitalization.

We recorded a total of 92 in-hospital deaths, corresponding to an in-hospital mortality rate of 26% among closed cases. Deaths occurred after a median of 7 (Q1-Q3 4–12) days from hospital admission. Fig. 1 depicts the probability of in-hospital death across age (Odds Ratio 1.10 per year increase, 95%CI 1.07–1.13). Variations in D-dimer levels among survivors and non-survivors are displayed in Table 2.

3.1. Use of thromboprophylaxis

All ICU patients received thromboprophylaxis with low-molecular-weight heparin: the dosage was weight-adjusted in 17 patients and therapeutic in two patients on ambulatory treatment with direct oral anticoagulants. A total of 246 (75%) patients admitted to general wards received initial in-hospital thromboprophylaxis: a prophylactic dosage was used in 133 (41%) patients, 67 (21%) were treated with intermediate-dosage thromboprophylaxis, and 74 (23%) received therapeutic-dose anticoagulation, including 22 who continued ambulatory treatment for atrial fibrillation or prior VTE.

3.2. Thromboembolic complications

Thromboembolic events occurred in 28 of 362 closed cases for a rate of 7.7% (95%CI 5.4%–11.0%) among closed cases, corresponding to a cumulative rate of 21.0%. Eight events occurred in ICU patients (16.7%; 95%CI 8.7%–29.6%) corresponding to a cumulative rate of 27.6%. Twenty events occurred in patients on the general ward (6.4%; 95%CI 4.2%–9.6%) corresponding to a cumulative rate of 6.6% (Table 3). We reported a detailed description of all thromboembolic events in Table 4.

Forty-four patients underwent VTE imaging tests and 16 were positive (36% of tests, 4.4% of total patients). Ten (63%) of 16 events were pulmonary embolism; 33% of CTPA were positive. In 8 (50%) of 16 patients with VTE, the VTE event was diagnosed within 24 h of hospital admission. Nine (56%) of these 16 patients were not receiving any anticoagulant treatment. One patient diagnosed with sub-segmental PE that occurred during anticoagulant prophylaxis had a D-dimer level (323 ng/mL) within the normal range, whereas the

Table 1
Baseline characteristics of COVID-19 patients.

	Intensive care unit (n = 61)		General ward (n = 327)		Total (N = 388)	
Age (years), median (Q1-Q3)	61 (55–69)		68 (55–77)		66 (55–75)	
Men	49/61	80.3%	215/327	65.7%	264/388	68.0%
Body mass index (kg/m2)						
≤25	20/57	35.1%	110/306	35.9%	130/361	36.0%
25–30	20/57	35.1%	126/306	41.2%	144/361	39.9%
≥30	17/57	29.8%	70/306	22.9%	87/361	24.1%
Overall duration of hospitalization (days), median (Q1-Q3)	18 (14–24)		9 (6–13)		10 (7–15)	
Cardiovascular risk factors						
Arterial hypertension on treatment	27/61	44.3%	156/327	47.7%	183/388	47.2%
Diabetes mellitus on treatment	11/61	18.0%	77/327	23.5%	88/388	22.7%
Dyslipidemia on treatment	7/61	11.5%	69/327	21.1%	76/388	19.6%
Chronic renal dysfunction	9/61	14.8%	52/327	15.9%	61/388	15.7%
Smoking	3/61	4.9%	42/327	12.8%	45/388	11.6%
Active cancer	2/61	3.3%	23/327	7.0%	25/388	6.4%
Solid	1		16		17	
Hematological	1		9		10	
Ongoing cancer therapy	1/61	1.6%	10/327	3.1%	11/388	2.8%
Hormonal therapy	1		3		4	
Chemo/immuno-therapy	0		5		5	
Radiotherapy	0		2		2	
History of cancer	0/61	0%	2/327	0.6%	2/388	0.5%
Chronic obstructive pulmonary disease	1/61	1.6%	34/327	10.4%	35/388	9.0%
Prior thromboembolic events						
Coronary artery disease	7/61	11.5%	47/327	14.4%	54/388	13.9%
Prior stroke	1/61	1.6%	19/327	5.8%	20/388	5.2%
Peripheral atherosclerosis	5/61	8.2%	48/327	14.7%	53/388	13.7%
Prior venous thromboembolism	0/61	0.0%	12/327	3.7%	12/388	3.1%
Use of co-medications						
Aspirin	17/61	27.9%	77/320	24.1%	93/379	24.5%
Vitamin K antagonists	0/61	0%	16/329	4.9%	16/388	4.1%
Direct oral anticoagulants	2/61	3.3%	15/329	4.6%	17/388	4.4%
ACE-inhibitors	6/61	9.8%	47/329	14.3%	53/388	13.7%

Chronic renal dysfunction was present if previously reported and with a baseline or anamnestic estimated glomerular filtration rate of < 60 mL/min. Active cancer was defined by the presence of metastatic or terminal cancer, or by active cancer therapy in the prior 3 months. ACE, angiotensin-converting enzyme.

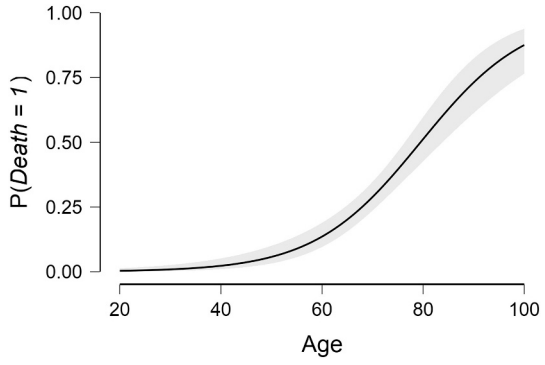

Fig. 1. Probability of in-hospital death across age.
We performed logistic regression to ascertain the effects of age on the likelihood that patients died during hospitalization (Odds Ratio 1.10; 95%CI 1.07–1.13). The figure depicts the probability of in-hospital death across age. The analysis was restricted to closed cases (dead or discharged at the time of analysis).

remaining 15 patients had values comprised between 1620 and 40,905 ng/mL. None of the patients diagnosed with acute PE or DVT had a history of VTE.

Ischemic stroke was diagnosed in 9 (2.5%) patients: 3 were on the ICU and 6 of those on the general ward. One patient developed both stroke and acute PE. In 6 (67%) patients, stroke was the primary reason for hospitalization. Acute coronary syndrome/myocardial infarction was diagnosed in four (1.1%) patients, of whom 3 were on the ICU and one of those on the general ward. This represented the primary reasons for hospitalization in 3 (75%) patients.

3.3. Disseminated intravascular coagulation

A total of 8 (2.1%) patients met the laboratory criteria for overt DIC. Six (75%) patients were men, one (13%) was required intensive care, four (50%) had solid or hematological cancer. No bleeding complications were recorded. Two (25%) patients had thromboembolic events (DVT, ischemic stroke); Table 4. Seven (88%) patients with overt DIC died during hospitalization.

4. Discussion

We performed a comprehensive analysis of the rate, timing, and characteristics of venous and arterial thromboembolic complications among consecutive COVID-19 patients admitted to a large university hospital in Milan, Italy. Our results indicate that thromboembolic complications may represent an integrating part of the clinical picture of COVID-19 and be already present at the time of initial hospital admission. Their incidence, however, may have been highly underestimated due to the low number of specific imaging tests performed. It remains unclear whether increased intensity of thrombosis prophylaxis in selected patients may provide clinical benefit in patients without confirmed acute VTE. Interventional and management trials should be conducted to improve the prevention, diagnosis, and treatment of thrombotic complications in these patients.

Previously, coagulation and cardiac biomarkers have been described to be elevated in COVID-19 patients: they reflect an inflammatory status characterized by coagulation activation and endothelial dysfunction, and are predictors of death [2–7,9]. We showed that, despite the use of anticoagulant prophylaxis, the rate of venous and arterial thromboembolic complications in hospitalized COVID-19 patients was remarkable, approximately 8%. Indeed, this already high

Table 2
Median D-dimer levels in survivors and non-survivors during hospitalization.

Group	Setting	Days 1–3	Days 4–6	Days 7–9
Survivors	Total	*n* = 215	*n* = 163	*n* = 121
		353 (236–585)	389 (246–685)	529 (303–1138)
	ICU	615 (456–1005)	605 (370–824)	3137 (1486–6571)
	General ward	329 (304–386)	378 (337–412)	472 (386–650)
Non-survivors	Total	*n* = 70	n = 38	*n* = 22
		869 (479–2103)	943 (611–2618)	1494 (633–6320)
	ICU	1022 (615–3681)	1301 (961–28,397)	7746 (2914–12,578)
	General ward	868 (600–1119)	847 (624–1643)	1093 (658–3397)

The analysis was restricted to closed cases. D-dimer levels are presented as median (Q1-Q3) and expressed in ng/mL. ICU, intensive care unit.

figure may represent an underestimation of the actual values. We postulate this based on four key findings: (i) VTE was actively searched in only 10% of COVID-19 patients, (ii) one third of VTE imaging tests were positive, (iii) more than half of venous or arterial thromboembolic events were diagnosed within the first 24 h of hospital admission, representing often the first manifestation of COVID-19, (iv) the vast majority of PE events was “unquestionable” from a radiological/anatomical perspective and no diagnosis was "incidental".

The observed rate of thrombotic events is in line with recent preliminary analyses, although the severity of patients and the use of thromboprophylaxis across studies were heterogeneous and may have influenced the estimates. In a recent Dutch paper, symptomatic VTE was diagnosed in 28 (15% of total; cumulative rate 27%) of 184 patients receiving thromboprophylaxis during intensive care and mainly consisted of PE ($n = 25$) [10]. In the Dutch study, only a minority of patients experienced arterial thrombotic events ($n = 3$). According to a Chinese study, the prevalence of VTE was 25% with routine VTE screening, although details on the type and timing of screening were not provided [11]. These values appear much higher than the rate of symptomatic VTE events observed in thromboprophylaxis trials, not exceeding 3% in patients not receiving anticoagulant therapy and < 1% on thromboprophylaxis [13], but in line with what observed in patients with sepsis or shock [14,15]. A recent analysis from a French group showed that the rate of thromboembolic complications in 150 COVID-19 patients with ARDS was much higher (11.7%) than what observed in a historical control group of non-COVID-19 ARDS patients (2.1%) despite anticoagulation [16].

We showed that the majority of thrombotic complications were venous and primarily represented by (isolated) PE. Consistently, the proportion of positive CTPA out of total CTPA performed (33%) appeared higher than that of positive CUS (21%) out of total CUS performed. As indirect as this evidence is, one may postulate that in case of suspected PE, the execution of CUS may be logistically more feasible but give less useful information and delay CTPA testing. It has been suggested that the use of higher prophylaxis dosages may improve the outcome of COVID-19 patients [10,17]. The results of our analysis suggest that a lower threshold of suspicion to perform VTE imaging tests may be reasonable, even upon admission or in the very early phases of COVID-19. We observed at least half of thromboembolic events were diagnosed within the first 24 h of admission and, therefore, not preventable by in-hospital thromboprophylaxis, which would have been otherwise inadequately dosed in the presence of acute VTE.

Routine thromboprophylaxis is not recommended in ambulatory patients with acute medical illness or respiratory symptoms [18]. It has been postulated that the administration of low-molecular-weight heparin during the earlier phases of SARS-CoV2 infection may exert a positive effect not only in terms of thrombosis prevention, but also reducing systemic and pulmonary inflammation, and limiting viral invasion [7,17,19–21]. In several country, a number of patients is being managed on an ambulatory basis, also for logistical reasons. The burden of thromboembolic complications in these patients is unknown. Our data, which represent conditional probabilities and should therefore be carefully interpreted, suggest that this may represent an underestimated, large-scale issue requiring rapid answers. A randomized controlled trial, the OVID trial, is being planned to study whether prophylactic-dose enoxaparin (*vs.* no treatment) may reduce early all-cause mortality and unplanned hospitalizations in adult symptomatic ambulatory COVID-19 patients with no other indications to receive anticoagulation.

We acknowledge limitations to our study. This was a retrospective analysis conducted at a large university hospital, therefore possibly not reflecting the management strategies and diagnostic facilities at other non-academic institutions. Patients included in this analysis were diagnosed at one of the “red zones” where the European outbreak started. This may have influenced not only patients' outcome, as no global experience on the disease was available yet, but also the execution and frequency of imaging tests during hospitalization. From this perspective, we could not confirm whether thromboembolic events contributed

Table 3
Venous and arterial thromboembolic events in hospitalized COVID-19 patients.

	Intensive care unit			General ward			Total		
Thromboembolic events	n	% of closed cases (n = 48)	% of imaging tests performed*	n	% of closed cases (n = 314)	% of imaging tests performed*	n	% of closed cases (n = 362)	% of imaging tests performed
At least one thromboembolic event	8	16.7% (95%CI 8.7%–29.6%)	–	20	6.4% (95%CI 4.2%–9.6%)	–	28	7.7% (95%CI 5.4%–11.0%)	–
VTE	4	8.3%	22%	12	3.8%	46%	16	4.4%	36%
PE (± DVT)	2	4.2%	25%	8	2.5%	36%	10	2.8%	33%
Isolated pDVT	1	2.1%	7%	3	1.0%	44%	4	1.1%	21%
Isolated dDVT	0	–	–	1	0.3%	13%	1	0.3%	13%
Catheter-related DVT	1	2.1%	50%	0	–	–	1	0.3%	50%
Ischemic stroke	3	6.3%	–	6	1.9%	–	9	2.5%	–
ACS/MI	1	2.1%	–	3	1.0%	–	4	1.1%	–

ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; pDVT, proximal deep vein thrombosis; dDVT, distal DVT; PE, pulmonary embolism; VTE, venous thromboembolism.

Table 4
Description of patients with thrombotic events.

Sex	Age	Cancer	Thromboprophylaxis at diagnosis	D-dimer[a]	Setting	Thromboembolic event	AC therapy	Outcome
F	45	–	No	1620	General ward	Proximal DVT	Enoxaparin 80 mg bid	Discharged
F	64	–	No	2371	General ward	Great saphenous vein thrombosis, junction thrombosis	Nadroparin 5700 IU bid followed by enoxaparin 40 mg bid	Discharged
M	71	–	Yes (P)	1842	ICU	Distal DVT	Fondaparinux 7.5 mg qd	Hospitalized
M	68	–	Yes (I)	4199	General ward	Smaller saphenous vein thrombosis, junction thrombosis	Fondaparinux 2.5 mg qd	Discharged
M	55	–	Yes (P)	1915	ICU	Subclavian-axillary catheter-related DVT	Fondaparinux 7.5 mg qd	Discharged
M	73	Lung small-cell carcinoma	No	5542	General ward	Proximal DVT, overt DIC	Nadroparin 5700 IU bid	Dead
M	86	–	Yes (P)	2270	General ward	Bilateral segmental PE	Nadroparin 5700 IU bid followed by cava filter placement after major bleeding	Dead
M	75	–	Yes (P)	323	General ward	Multiple subsegmental PE	Enoxaparin 60 mg bid	Hospitalized
F	67	Pancreas carcinoma	No (Aspirin)	2563	General ward	Unilateral lobar PE	Nadroparin 5700 IU bid	Dead
F	78	–	No (Aspirin)	40,950	General ward	Bilateral PE, proximal DVT	Enoxaparin 8000 IU qd followed by edoxaban 60 mg qd	Discharged
F	69	Diagnosis pending	No (Aspirin)	3527	General ward	Bilateral segmental PE	Enoxaparin 4000 IU bid	Discharged
M	78	–	No	37,176	General ward	Unilateral segmental PE	Nadroparin 7600 IU bid	Discharged
M	59	–	Yes (P)	4523	ICU	Inferior vena cava thrombosis with clot in right atrium and suspected PE	Nadroparin 9500 IU bid	Discharged
M	59	–	Yes (P)	3123	ICU	Bilateral PE, subclavian and jugular DVT	Enoxaparin 60 mg bid	Discharged
M	55	–	None	3636	General ward	Bilateral lobar PE	Enoxaparin 90 mg bid	Discharged
M	67	Metastatic lung carcinoma	Yes (I)	8608	General ward	Stroke, PE	Local lysis and mechanical thrombectomy; PE: enoxaparin 60 mg bid	Discharged
F	71	–	Yes (P)	408	General ward	NSTEMI	Prasugrel followed by clopidogrel + indobufen + enoxaparin 40 mg bid	Discharged
F	82	Metastatic breast cancer	Yes (P)	3000	General ward	NSTEMI	Aspirin	Dead
F	65	–	Yes (I)	3187	ICU	NSTEMI	Aspirin + enoxaparin 40 mg qd (negative coronary angiogram)	Discharged
M	78	Larynx carcinoma	No	340	General ward	STEMI	None	Dead
M	67	–	Yes (I)	6435	ICU	Stroke (no atrial fibrillation)	Aspirin	Discharged
F	76		Yes (T)	–	General ward	Stroke (no atrial fibrillation)	Aspirin + nadroparin 5700 IU bid	Dead
M	64	–	No (Aspirin)	677	General ward	Stroke (no atrial fibrillation)	Systemic thrombolysis, aspirin + nadroparin 3800 IU qd	Discharged
M	68	–	No (Aspirin)	280	General ward	Stroke (no atrial fibrillation)	Clopidogrel + nadroparin 3800 IU qd	Hospitalized
M	69	–	–	249	ICU	Stroke (atrial fibrillation)	Mechanical thrombectomy, aspirin followed by therapeutic-dose heparin (AF)	Hospitalized
M	57	–	Yes (P)	6071	ICU	Stroke (no atrial fibrillation), necrotizing meningoencefalitis	Therapeutic-dose unfractionated heparin	Hospitalized
F	73	–	Yes (Acenocoumarol INR 1.2)	1158	General ward	Stroke (atrial fibrillation)	Systemic thrombolysis, therapeutic-dose nadroparin	Discharged
F	75	Lung carcinoma	Yes (I)	61,000	General ward	Stroke, DIC	Nadroparin 5700 IE	Dead

[a] On the day of thrombosis or closest available. AF, atrial fibrillation; bid, twice daily; DIC, disseminated intravascular coagulation; DVT, deep vein thrombosis; F, female; ICU, intensive care unit; INR, international normalized ratio; PE, pulmonary embolism; M, male; qd, once daily. Thromboprophylaxis dosage: (P) prophylactic; (I) intermediate (including weight-adjusted); (T) therapeutic.

substantially to such a dramatic mortality and no autopsies were routinely performed in COVID-19 patients. Indeed, we showed that the D-dimer levels, a marker of inflammation and coagulation activation, rapidly increased in non-survivors during the course of hospitalization; overt DIC was present in 2% of COVID-19 patients and fatal in almost all cases.

5. Conclusions

Hospitalized patients with COVID-19 were characterized by substantial in-hospital mortality and a high rate of thromboembolic complications. Rapidly increasing D-dimer levels were observed in non-survivors, reflecting the inflammatory and procoagulant state of COVID-19. The high number of arterial and, in particular, venous thromboembolic events diagnosed within 24 h of admission and the high rate of positive VTE imaging tests among the few COVID-19 patients tested suggest that there is an urgent need to improve specific VTE diagnostic strategies and investigate the efficacy and safety of thromboprophylaxis in ambulatory COVID-19 patients.

Declaration of competing interest

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